

## **REMARKS**

### **The Rejections**

Claims 1, 3-4, 7-8 and 10-14 are rejected under 35 USC 103(a) as being unpatentable over Lee et al. (Journal of Polymer-Science, Part A: Polymer Chemistry, Vol. 39, 973-985, 2001) in view of Seo et al. (WO 03/033593). Claims 5 and 9 appear to be rejected under 35 USC 103(a) as being unpatentable over Lee et al. in view of Seo et al. and in view of Sodergard (US 2004/0091573). Clarification of exactly which claims are included in this rejection is requested from the Examiner in the next Office Action. These rejections are respectfully traversed.

### **Argument**

The present invention relates to a micellar composition (and a method of preparing a polylactic acid derivative) comprising a water-soluble polylactic acid derivative which can form stable micelles and increase the solubility of poorly water-soluble drugs by entrapping the drugs in micelles. The present invention stabilizes micelles by increasing the molecular weight of the polymer which is used to form the micelles and accordingly lowering the critical micelle concentration (CMC). If CMC is too high, more polymer is required to form micelles and then the micelles become unstable, which results in precipitation of poorly water-soluble drugs. If the molecular weight of a linear PLA salt increases, it becomes more difficult to dissolve in water. The present inventors have designed a multiarm polymer structure wherein the total molecular weight increases but that of each PLA arm does not, while the water solubility is maintained.

The present invention seeks to provide a stable micellar composition. In the Lee et al. reference, the degradation rate of COOH terminated polylactide is higher than those having other terminals, and among the COOH-terminated polylactides, 3- or 4-armed COOH-terminated PLA has a higher degradation rate than linear PLA (see the Abstract and Fig. 6). This is because the hydrolysis of the polymer backbone is accelerated by the presence of the terminal acid group

(COOH), and accordingly 3- or 4-armed PLA, which has more acid groups, is degraded more rapidly (please see the right column, P982 of the Lee et al. reference).

However, the present invention relates to a micellar composition providing micelles with increased stability in order to entrap and maintain hydrophobic drugs therein. Furthermore, the terminal of the present polymer is in a salt form and not an acid form. The Lee et al. reference teaches away from the increased stability of the polymer in the present invention since the Lee et al. reference teaches that more accelerated degradation of the polymer can be achieved by more multi-arms of the polymer.

The Examiner also alleges that the micellar formation is obvious from the combination of the Lee et al. and Seo et al. references. However, the Seo et al. reference just mentions low-molecular weight and linear polymers. The Seo et al. reference fails to provide any expectation as to whether its polymer can maintain the water solubility when it becomes a multi-armed form with higher molecular weight. The Lee et al. reference discloses a water-insoluble and high molecular weight polymer having about 33,200 Daltons. Therefore, even if the prior art is combined, one skilled in the art could not have easily modified the molecular weight of the polymer to arrive at the present invention. Whether a polymer is soluble or insoluble in water should be regarded as an important factor of polymer properties. It is never a simple modification of numerical ranges or ratios.

Since the Sodergard reference does not fill the deficiencies of either the Lee et al. or Seo et al. references, the further reliance upon the Sodergard reference cannot possibly suggest the present invention.

Accordingly, in view of the above remarks, reconsideration of the rejections and allowance of all of the claims of the present application are respectfully requested. In the event that the present Request for Reconsideration does not place the present application into condition for allowance, entry thereof is respectfully requested as placing the present application into better condition for appeal.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Joseph A. Kolasch, Registration No. 22463, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By 

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